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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,721	02/12/2001	H. Michael Shepard	NB 2004.02; 060925-0402	5394

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
11/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/782,721	SHEPARD ET AL.	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 21, 2007(amdt)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,57,62 and 91-94* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56,57,62 and 91-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/05/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims **1-55, 58-61 and 63-90** have been cancelled, claims **56, 57 and 62** have been amended, the disclosure has not been further amended, and new claims **91-94** has been added as per the amendment filed August 21, 2007, an amendment filed to effect requested changes in the amendment filed August 6, 2007. One additional Information Disclosure Statement (1 IDS) filed September 9, 2007 has been received with the single cited reference and made of record. Applicant's submission of a list of related cases is noted with appreciation.

Claims **56, 57, 62 and 91-94** remain in the case.

Note to applicant: When a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **56, 57, 62 and 91-92** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims **56 and 57** are directed to methods of "inhibiting" and "treating," respectively, wherein the particular disease to be inhibited or treated has been specified as a list of disease cell types, the cell types being breast, non-small cell lung, rectal, head and neck, stomach, pancreatic, colon, liver, gastric (same as stomach?), and ovarian. This laundry list of organ-related cell types only may meet the written description requirement when the cell is derived from breast, colon or lung in view of the instant disclosures wherein these tissues have been tested as disclosed in Tables found at pages 72 and 76 of the disclosure. For the other listed types of neoplastic cell types, the written description has not yet been met.

Claims **62 and 91-92** are directed to compounds actually tested and to other compounds encompassed by the terminology at lines 40-43 wherein all manner of stereoisomers are encompassed. While applicant clearly has support for the D-ribosyl compounds, esters, ethers and salts, there is no support for the remainder of the alternatives either in the area of synthesis or the area of pharmacological testing. It is well known that stereoisomerism can have profound effect on pharmacological activity (e.g. the enantiomer of morphine apparently has no pharmacological effects in humans; the enantiomer of "speed" is the well known nasal

decongestant pseudoephedrine). Therefore, applicant is respectfully requested to either submit additional data (1.132 declaration) to support the allegations of anti-neoplastic activity of non-D-ribosyl isomers or to delete these alternatives from the claim.

Applicant's arguments filed August 21, 2007 have been fully considered but they are not persuasive.

Examiner has reviewed the record in this case and does not recall, and could not readily locate any prior art reference wherein the argument is made that a neoplasm located at one organ will, or will not, migrate through the circulatory system to another organ and establish by a kind of infection a neoplasm feeding on another type of tissue. Examiner is also not aware of what types of neoplasms are more likely to behave in this manner. Examiner has reviewed the newly submitted **Smith et al.** reference, a disclosure that suggests the possibility of classifying neoplasms according to their ease of culture and ease of cloning, aptitudes that may, or may not, be related to the aptitude to migrate and "infect" other tissues (establish metastases). If applicant is aware of any prior art (already cited or not yet cited) dealing with or elucidating these aptitudes, examiner would like same to be of record as a possible basis for findings that are not strictly limited to the specific test exemplifications. The above amended grounds of rejection reflects the limited capability to address the problem of establishing a factual basis for determination of which neoplasms can be treated and which are not treatable with the instant claimed compounds.

The second part of the above rejection is a new ground of rejection and therefore properly a reason to make this Office action non-final.

Claims **56-57** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for certain breast neoplasms, colon neoplasms and lung neoplasms, does not reasonably provide enablement for any of the other varieties of neoplasms now listed in the claims **56 and 57**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in In re Wands (858 F.2d 731, 737; 8

USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims as defined by the lists of neoplastic cell types is excessively broad because said term reads on multiple different disease conditions including all varieties of neoplasms (cancers cells). Only claims **93 and 94** are limited to generic classes of neoplastic cell types including enabled specific neoplastic diseases.

B. The nature of the invention as described in the specific examples is limited to a showing that a single compound, a phosphoramidated derivative of 5-bromovinylated 2'-deoxyuridine nucleoside is much more effective that the non-phosphoramidated BVDU base compound in treating certain specific neoplastic diseases, human breast carcinoma, a specific strain of lung cancer, and human colon carcinoma in particular.

C. The state of the prior art; the extensive prior art of record, as presently understood and reviewed, does not anticipate or render obvious the treatment of carcinomas with a phosphoramidated BVDU.

D. The level of one of ordinary skill is defined by the need to understand organic synthesis, and the testing of compounds in *in vitro* cell culture.

E. The level of predictability in the art is low because only two closely related neoplastic disease conditions have been shown to be effectively inhibited by a phosphoramidated BVDU compound.

F. The amount of direction provided by the inventor is limited to showing how to make and administer a single phosphoramidated BVDU compound to cause inhibition of three neoplastic disease conditions.

G. The existence of working examples is limited to a single compound administered to cells in in vitro culture infected by three neoplasms all of which are probably carcinomas.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure would be excessive because the disclosure does not described how to effectively treat anything other than carcinoma in humans breast, human lung, and human colon tissue.

Applicant's arguments filed August 21, 2007 have been fully considered but they are not persuasive.

The above rejection has been amended in response to applicant's amendment. Applicant is referred to the response to arguments following the preceding rejection.

Claim **62** is objected to because of the following informalities:

In claim **62** at lines 40-43, the term "any enantiomeric, diastereomeric ... or any stereoisomeric form" appears to include two repetitions ("enantiomeric" and "stereoisomeric form") directed to subject matter also encompassed by the term "a D-form and an L-form."

Appropriate correction is required.

Applicant's arguments with respect to claim **62** have been considered but are deemed to be moot in view of the new grounds of objection.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim ***1-12*** of U. S. Patent No.

6,495,553. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***36-39*** of U. S. Patent No. **6,339,151**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-7*** of U. S. Patent No. **6,245,750**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***7-30 and 37-40*** of co-pending Application No. **10/119,927**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 and 53-83*** of co-pending Application No. **10/681,418**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-10*** of U. S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-19*** of co-pending US Application No. **10/048,033**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***15-18, 21-23 and 27-50*** of co-pending Application No. **09/789,226**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-53*** of co-pending Application No. **11/034,036**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **56, 57 and 93-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 and 2*** of U. S. Patent

No. **7,138,388** (See PTO-892 for citation). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Claims **56, 57, 62 and 91-94** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 -20*** of co-pending Application No. **11/516,457**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

One or more of claims **56, 57, 62 and 91-94** of this application conflict with claims ***7-30 and 37-40*** of Application No. **10/119,927**, claims ***1 and 53-83*** of co-pending Application No. **10/681,418**, claims ***1-36*** of copending Application No. **11/034,036**, and claims ***1-20*** of copending Application No. **11/516,457**, claims ***1-19*** of co-pending US Application No. **10/048,033**, and claims ***15-18, 21-23 and 27-50*** or copending Application No. **09/789,226**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

Applicant's arguments filed August 21, 2007 have been fully considered but they are not persuasive.

Applicant has acknowledged but has deferred effective responses to some of the above obviousness-type double patenting grounds of rejection. No terminal disclaimers have yet been received citing the above applications and patents. The rejections have been reconsidered as requested by applicant and found to remain valid. Therefore, the instant grounds of rejection found in the previous Office action have been maintained.

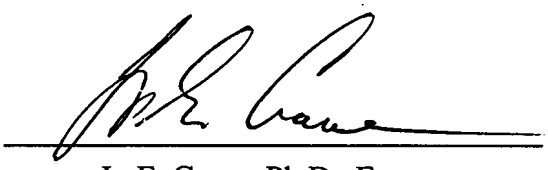
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX directly to Examiner's computer is 571-273-0651. The telephone number for submission of an official FAX to the USPTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
10/29/2007



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